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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P. 1940 DUKE STREET ALEXANDRIA, VA 22314				MUMMERT, STEPHANIE KANE
ART UNIT		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/537,000	VOLLAND ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 12 November 2009.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 28,29 and 31-54 is/are pending in the application.  
 4a) Of the above claim(s) 45 and 47-54 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 28,29,31-42 and 46 is/are rejected.  
 7) Claim(s) 43 and 44 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
     1. Certified copies of the priority documents have been received.  
     2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
     3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____.   | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

Applicant's amendment filed on November 12, 2009 is acknowledged and has been entered. Claims 1-27 and 30 have been canceled. Claims 28-29, 31-33-44 and 46 are pending. Claims 45 and 47-54 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 28-29, 31-44 and 46 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**This action is made FINAL.**

### **Status Identifiers**

It is noted that claim 41 is listed as "Currently Amended", but no amendment to the claims has been made. Correction is requested.

### **Previous Grounds of Rejection**

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 31-42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al. (US Patent 5,851,778; December 1998) in view of Ballerstadt et al. (Analytica Chimica Acta, 1997, vol. 345, p. 203-212) and Groopman et al. (PNAS, 1984, vol. 81, p. 7728-7731). Oh teaches a method of detection of target analytes using a capture member immobilized on a solid support through a trifunctional linker and detection of fluorescence (Abstract).

With regard to claim 28, Oh teaches a method for detection of an analyte a in a fluid sample, comprising the following steps:

1) saturating a solid support comprising, on at least part of its surface, at least one trifunctional reagent (tripod Y) (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as “the tridentate members operate pursuant to certain steric properties”; see Figure 11, where the space molecule is attached to a solid support; see also Example 7 and 8) comprising the following three functional poles:

i) a luminescent group (L) (Figure 11, Example 8, where DNP is labeled with a anti-DNP

antibody labeled with fluorescein (proximity label); see also isoluminol proximity label on the solid support);

ii) a molecule (B) selected from the group consisting of the analyte a, an analog of the analyte a or a fragment of the analyte a, which can non-covalently and reversibly bind a receptor specific for the analyte (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample); and

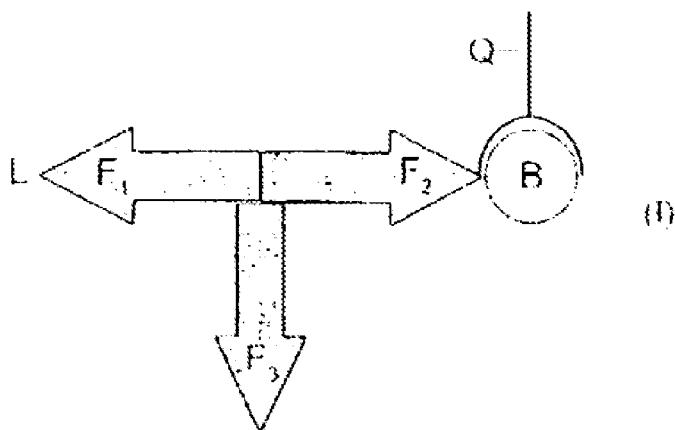
iii) a function that provides attachment of the trifunctional reagent to the surface of the solid support (see Figure 11, where the spacer tridentate molecule is attached to a solid support; see also Example 7 and 8);

2) bringing the solid support obtained in step 1) into contact with a fluid sample that may comprise the analyte a to be detected (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample; see col. 39, 'assay for analyte' heading, lines 8-20).

With regard to claim 33, Oh teaches an embodiment of claim 28, wherein the fluid sample is water, a liquid biological medium, or a liquid medium comprising dissolved gaseous molecules or molecules originating from solid samples (col. 39, lines 8-10, where the sample is a liquid sample comprising analyte).

With regard to claim 34, Oh teaches an embodiment of claim 28, wherein the intensity of the signal emitted during step 3) is determined by a luminescence detector (col. 39, line 8-15, where the sample is assayed using a luminometer, which detects luminescence).

With regard to claim 35, Oh teaches an embodiment of claim 28, wherein the complex C formed at the end of the saturation in 1) is selected from the group consisting of complexes of formula (I) below:



wherein:

- the arrows represent the structure of the backbone of the tripod Y, which is a linker arm which is a peptide, nucleotide or glucoside chain or of a saturated or unsaturated, linear or branched hydrocarbon-based chain; the chains being optionally substituted, interrupted and/or ended with one or more hetero atoms, selected from the group consisting of N, O and S, and/or with one or more amino acids, and comprising three reactive chemical functions F1, F2 and F3 (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as “the tridentate members operate pursuant to certain steric properties”; see Figure 11, where the spacer molecule is attached to a solid support; see also Example 7 and 8; see also col. 18, lines 51-63); the molecule (B) being covalently bonded to the tripod Y by the reactive chemical function F2 (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay

measures the presence of theophylline in a sample; see Example 4, where the details of the functional groups are provided);

- L represents the luminescent group covalently bonded to the tripod Y by the reactive chemical function F1 (isoluminol proximity label on the solid support renders the covalently attached luminescent group obvious; see also Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label));
- F3 represents a reactive chemical function through which the tripod Y is attached to the surface of the solid support (Figure 11, Example 8, the tripod is attached to the solid support and comprises functional groups for attachment; see col. 18).

With regard to claim 36, Oh teaches an embodiment of claim 35, wherein the functions F1, F2 and F3, independently of one another, provide:

- i) either a direct linkage via a corresponding chemical function present on the luminescent compound, the molecule (B) or the solid phase (Figure 11, Example 7 and 8, where the tripod/tridentate is attached to the solid support and comprises functional groups for attachment; see col. 18 and Example 4, ‘attachment of third tridentate member’ where the tridentate comprises amine functional groups associated with the lysine based spacer);
- ii) or an indirect linkage, wherein the linkage is carried out by coupling, to at least one of the functions F1, F2 and/or F3, a molecule M1 forming a complex with a molecule M2 attached beforehand to at least part of the surface of the solid phase, to the molecule (B) and/or to the luminescent group (isoluminol proximity label on the solid support renders the attached luminescent group obvious; see also Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label)).

With regard to claim 37, Oh teaches an embodiment of claim 35, wherein the functions F1, F2 and F3, which may be identical or different, are selected from the group consisting of: thiols; amines; alcohols; acid functions; esters; isothiocyanates; isocyanates; acylazides; sulfonyl chlorides; aldehydes; glyoxals; epoxides; oxiranes; carbonates; imidoesters; carbodiimides; maleimides; nitriles; aziridines; acryloyl; halogenated derivatives; disulfide groups; phosphorus-containing groups; diazo; carbonyldiimidazole; hydrazides; arylazides; hydrazines; diazirines; magnesium compounds; lithium compounds; cuprates; zinc compounds and unsaturated systems (see col. 18 and Example 4, ‘attachment of third tridentate member’ where the tridentate comprises amine functional groups associated with the lysine based spacer).

With regard to claim 38, Oh teaches an embodiment of claim 37, wherein the functions F1, F2 and F3 are selected from the group consisting of amine functions of formulae R- NH<sub>2</sub>, R-NH-, (R)<sub>3</sub>-N, R-NH-OR and NH<sub>2</sub>-OR; alcohol functions R-OH; and halogenated groups of formula R-X with X representing a halogen atom; wherein R represents an alkyl, aryl, vinyl or allyl radical (see col. 18 and Example 4, ‘attachment of third tridentate member’ where the tridentate comprises amine functional groups associated with the lysine based spacer).

With regard to claim 39, Oh teaches an embodiment of claim 28, wherein the luminescent group is selected from the group consisting of fluorescein and its derivatives; rhodamine and its derivatives; diaminidophenyl indo; acridine; fluorescent dyes with reactive amines; eosin; and erythrosine (isoluminol proximity label on the solid support renders the attached luminescent group obvious; see also Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label)).

With regard to claim 40, Oh teaches an embodiment of claim 28, wherein the receptor is selected from the group consisting of whole antibodies, antibody fragments, or recombinant antibody forms, biological receptors, nucleic acids, peptide nucleic acids, lectins, transporter proteins, chelates and synthetic receptors (Figure 11, Example 8, where theophylline analog/analyte is present on the structure and where the assay measures the presence of theophylline in a sample; see claim 18, where the modulating member comprises an analyte or analyte analog and the binding partner comprises an antibody).

With regard to claim 41, Oh teaches an embodiment of claim 28, wherein the receptor exhibits greater affinity for the analyte a than for the molecule (B) (Figure 11, Example 8, where theophylline analog/analyte is present on the structure and where the assay measures the presence of theophylline in a sample; see claim 18, where the modulating member comprises an analyte or analyte analog and the binding partner comprises an antibody).

With regard to claim 46, Oh teaches a method for continuous heterogeneous-phase detection of an analyte a in a fluid sample, comprising detecting the analyte a in a fluid sample with at least one complex C of formula (I) according to claim 35 (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample).

Regarding claim 28, 33-41 and 46, Oh does not teach that the analyte specific receptor was labeled with a compound that quenches luminescence. Ballerstadt teaches a fluorescence quenching affinity assay for the detection of lectins (Abstract).

With regard to claim 28, Ballerstadt teaches a receptor for analyte a (Abstract, Figure 1 and legend, where analyte a is a sugar and binds to a receptor, a lectin) and where the receptor is

labeled with a compound (Q) that quenches the luminescence of the group L, thereby forming a complex C between the molecule and the receptor-Q (the receptor binds to two molecules labeled with a fluorophore, fluorescein, and a quencher, rhodamine, which could be considered labels for the bivalent receptor; the polymers are crosslinked when the receptor is empty and the FRET labels quench each other in the absence of analyte a);

3) measuring the intensity of the signal emitted by the group L, which is proportional to the amount of analyte a present in the fluid sample (Figure 1 and legend, where when the analyte is present, the crosslinking and quenching between the polymer labels of the receptor is decreased and therefore the signal emitted by the fluorophore, fluorescein, is proportional to the amount of analyte a in the sample); and

4) regenerating the solid support by bringing the solid support into contact with the receptor-Q (Figure 1, where the "solid support" of the receptor-Q-lectin-receptor-L complex can be regenerated by the reversibility of the reaction; see Abstract, p. 205, col. 1, where the reaction between the receptor, the labels and the analyte are termed "elementary reversible reactions"; see also p. 211, col. 2, where "the assay is used as a reversibly working sensor", and p. 212).

With regard to claim 35, Ballerstadt teaches components of the structure of complex C, comprising:

-the receptor specific for the analyte a is non-covalently and reversibly attached, wherein the receptor is labeled with a compound Q (Abstract, Figure 1 and legend, where analyte a is a sugar and binds to a receptor, a lectin, which is labeled with a dextran labeled with a quencher, rhodamine);

- Q represents the compound that quenches the luminescence of the group L (Figure 1 and legend, where in this instance, the rhodamine quenches the luminescence of the group L on the other label for the receptor, dextran labeled with fluorescein).

With regard to claim 42, Ballerstadt teaches an embodiment of claim 28, wherein the quenching compound (Q) is selected from the group consisting of rhodamine and its derivatives, the fluorescent compounds mentioned in claim 12, and nonfluorescent molecules (Abstract, Figure 1 and legend, where analyte a is a sugar and binds to a receptor, a lectin, which is labeled with a dextran labeled with a quencher, rhodamine).

Regarding claim 28, while Ballerstadt teaches regeneration of the assay, Ballerstadt does not teach a solid support and instead teaches a homogeneous assay. Regarding claim 31-32, while Oh teaches a solid support, Oh is not explicit regarding the details of the solid support. Groopman teaches regeneration of solid supports useful in immunoassays (Abstract).

With regard to claim 28, Groopman teaches 4) regenerating a solid support (p. 7730, col. 2, where the solid support was regenerated using a wash; see also p. 7731, col. 1).

With regard to claim 31, Groopman teaches an embodiment of claim 28, wherein the solid support is selected from the group consisting of glasses, plastics, ceramics, metals and metalloids (p. 7729, col. 2, where the solid support comprised an affinity column).

With regard to claim 32, Groopman teaches an embodiment of claim 28, wherein the solid support is in the form of a tube, a capillary, a plate or a bead (p. 7729, col. 2, where the solid support comprised an affinity column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the competitive quenched format of detection taught by

Ballerstadt to the solid phase receptor based format of immunoassay taught by Oh to arrive at the claimed invention with a reasonable expectation for success. In Oh, proximity assays are carried out between a proximity label associated with a small molecule ligand, DNP, which is very similar to the receptor for the analyte, labeled with a quencher, as claimed (see Figure 11, Example 8). Oh differs from the instant claims because the receptor for the analyte is not labeled and the end resulting signal is achieved in a different way. First, it would have been obvious in view of the combination of proximity labels between a small molecule ligand and a labeled receptor. However, it is also noted that Ballerstadt teaches a homogeneous assay where the receptor for analyte a, a lectin, is labeled with dextran molecules labeled respectively with a fluorophore, fluorescein, and a quencher, rhodamine. In the absence of analyte, the lectin receptor crosslinks the dextran labels and the fluorescent signal is quenched through FRET interaction between the labels. However, where when the analyte is present in the sample, the crosslinking and quenching between the polymer labels of the receptor is decreased and therefore the signal emitted by the fluorophore, fluorescein, is proportional to the amount of analyte a in the sample. As taught by Ballerstadt, the “measuring principle relies on the fact that one portion of the dextran is coupled with an emitter dye fluorescein isothiocyanate (FITC), and the other one with an acceptor dye (isothiocyanate-derivatives of rhodamine). In absence of a specific sugar, the bridging of rhodamine and fluorescein-labeled dextrans by the lectin results in the formation of a sandwich-like fluorescein-dextran/lectin/rhodamine-dextran complex in which the two forms of dextran are very close together (~5 nm) so that fluorescence resonance energy transfer (FRET) occurs between fluorescein and rhodamine. Hence the fluorescence is quenched. The displacement of dextrans by a specific sugar results in the dissociation of the complex and in

an inverse *increase in fluorescence which is proportional to the sugar concentration.*" (Abstract, emphasis added). Furthermore, while Ballerstadt is a homogeneous assay and Oh teaches a heterogeneous assay, the two complimentary methods of proximity assay incorporating the interaction between fluorescent labels and quenchers, the labeling and detection format of Ballerstadt is applicable to both homogeneous and heterogeneous assays. Furthermore, as noted above, Ballerstadt also teaches that the reaction is reversible, and therefore that the receptor is regenerated. For example, Ballerstadt teaches "the assay is used as a reversibly working sensor" (p. 211, col. 2). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the competitive quenched format of detection taught by Ballerstadt, and the reversibility of the sensor, to the solid phase receptor based format of immunoassay taught by Oh to arrive at the claimed invention with a reasonable expectation for success.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Ballerstadt and Oh to include the solid supports as taught by Groopman and the regeneration of a support as suggested by Groopman to arrive at the claimed invention with a reasonable expectation for success. As taught by Groopman, "the antibody column was regenerated by washing the column with Pi/NaCl (pH 7.4); to date, we have used and regenerated this column more than 25 times with no apparent loss of activity" (p. 7730, col. 2). Groopman also teaches, "we have also found that when this antibody is bound to a solid-phase matrix, a reusable column can be prepared that selectively isolates aflatoxins from complex mixtures, such as urine, serum and milk" (p. 7731, col. 2). Therefore, one of ordinary skill in the art at the time the invention was made would have been

motivated to have adjusted the teachings of Ballerstadt and Oh to include the solid supports as taught by Groopman and the regeneration of the support as taught by Groopman to arrive at the claimed invention with a reasonable expectation for success.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable Oh et al. (US Patent 5,851,778; December 1998) in view of Ballerstadt et al. (*Analytica Chimica Acta*, 1997, vol. 345, p. 203-212) and Groopman et al. (PNAS, 1984, vol. 81, p. 7728-7731) as applied to claims 28, 30-42 and 46 above and further in view of Plowman et al. (*Analytical Chemistry*, 1999, vol. 71, p. 4344-4352). Oh teaches a method of detection of target analytes using a capture member immobilized on a solid support through a trifunctional linker and detection of fluorescence (Abstract).

Regarding claim 29, Oh teaches tripods Y (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as “the tridentate members operate pursuant to certain steric properties”; see Figure 11, where the space molecule is attached to a solid support; see also Example 7 and 8). However, neither Oh nor Lee teaches multiple types of tripods or the detection of multiple analytes.

With regard to claim 29, Plowman teaches an embodiment of claim 28, wherein several types of tripods Y that differ from one another through the nature of the molecule (B) that they comprise are attached to distinct and known zones of the solid support (Abstract, Figure 1, Table 2, where the method is applied to the detection of multiple analytes and therefore different formats of the reagent attached to the solid support).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the detection of multiple targets as taught by Plowman to the method of detection taught by Oh and Ballerstadt to arrive at the claimed invention with a reasonable expectation for success. As taught by Plowman, “Multiple analyte immunoassay (MAIA) results for two sets of three different analytes, one employing polyclonal and the other monoclonal capture antibodies, where compared with the results for identical analytes performed in a single analyte immunoassay (SAIA) format” (Abstract). Plowman therefore teaches the detection and analysis of multiple analytes in an immunoassay format similar in practice to the methods of Oh and Lee. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the detection of multiple targets as taught by Plowman to the method of detection taught by Oh and Ballerstadt to arrive at the claimed invention with a reasonable expectation for success.

### ***Response to Arguments***

Applicant's arguments, filed November 12, 2009 with respect to claims 28-29, 31-44 and 46 have been considered but are not persuasive.

Applicant traverses the rejection of claims 28, 31-42 and 46 as being obvious over Oh in view of Ballerstadt and Groopman. Applicant argues that the combination of references does not describe the claimed trifunctional reagent, “a regeneration of the solid support carrying 3) and 4) continuously”, “measuring the intensity of a signal emitted by a luminescent group L on a solid support, which is proportional to the amount of an analyte”. Applicant concludes that “one would have not been motivated to combine the methods of Oh et al., Ballerstadt et al., and

Groopman et al. Because the references describe different technologies the combination of which is improper” (p. 11 of remarks).

Applicant describes the method of claim 28, as including attachment of “the trifunctional reagent to the surface of the solid support” and as including a receptor which forms “a complex C between the molecule (B) and the receptor-Q”. Applicant further summarizes the steps of the method and provides a schematic of the instant invention in “Scheme A” (p. 13 of remarks).

Applicant argues “the signal is measured in the region on which tripod Y was immobilized, which makes it possible to obtain a localized signal” and “since the signal is localized, several molecules may be detected simultaneously on the same solid support” and “the presence of analyte a in the sample results in the appearance of a signal” (p. 14-15 of remarks).

Regarding Oh, Applicant summarizes the format of the reference. Principally, Applicant argues “a luminescent molecule or isoluminol is directly linked to the solid support” and “thus, it cannot be said that the reagent comprises a luminescent group” (p. 16 of remarks). Applicant argues that “luminescence is inversely proportional to the concentration of analyte” (p. 18 of remarks). Applicant also argues “the step of regeneration of the solid support of Oh, et al. Cannot be performed continuously” (p. 19 of remarks).

Regarding Ballerstadt, Applicant argues the combination is improper and would not lead to the method. Applicant argues that Ballerstadt describes a method carried out in solution (p. 19 of remarks). Applicant summarizes the method of Ballerstadt and effectively argues “even in the absence of the (sugar) analyte A, the situation in the solution is more complex than described in the abstract” and “only the P<sub>F</sub>R<sub>P</sub><sub>R</sub> complex... is a quenching effective complex” (p. 20 of remarks). Applicant argues that the signal produced can not be proportional and concludes that

for a variety of reasons related to the specific details of the method described by Ballerstadt, “one would not have been motivated to adapt the Oh et al. System to the Ballerstadt reactants with a reasonable expectation of achieving the claimed method” (p. 23 of remarks).

Finally, Applicant argues that the regeneration taught by Groopman “is different than that claimed” and that the method of Oh “cannot be combined with a thorough washing of the column in a manner which could be qualified as 'continuous'" (p. 26 of remarks).

These arguments have been considered, but are not persuasive. First of all, Applicant's arguments are focused on particular features of the invention, including the placement of the luminescent group, that the trifunctional reagent is present in the form of a tripod structure and that the receptor is attached to the support. In light of the specific limitations of the claim, it is argued in response that the “trifunctional reagent” is not necessarily a three armed structure and it is also not necessarily directed to the “tripod Y” format argued, or as depicted in Scheme A, for example. The claim merely requires that the reagent includes a luminescent group, an antigen and that it is attached in some way to a solid support, not that it must be in a three armed configuration as argued. Next, it is noted that, despite Applicant's arguments to the contrary, the key feature of the receptor is also not required to be attached to the complex, only that it “can noncovalently and reversibly bind to the analyte. Therefore, Applicant's arguments are not persuasive primarily because they are not directed to the scope of the claims as currently recited. Instead, the elements of the method of detection taught by Oh, in combination with Ballerstadt and Groopman render obvious for the reasons stated in the rejection above. The format of the assay of Oh, for example, is interpreted as functionally equivalent to the “trifunctional reagent”

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of the claims and therefore Applicant's arguments against Oh, Ballerstadt and Groopman are not persuasive and the rejection is maintained.

Furthermore, to briefly address the specifics of Applicant's remarks, it is noted that the isoluminol label on the solid support renders obvious a luminescent group anywhere on the structure because, as noted in Oh and as required by the instant invention, the luminescent group serves as a proximity label, regardless of where it is attached on the support.

Next, while Applicant's arguments against the alternative embodiment of the luminescent label on the anti-DNP antibody are acknowledged, in response it is noted that the anti-DNP label comprises a luminescent group as part of the support, as claimed within the method. Further, claim 28 does not require that the receptor for analyte a must be bound to the support alongside the luminescent label - only that it is capable of binding. Also, it is noted that while applicant's argument that the signal in Oh is inversely proportional, it is noted that Oh is not relied upon for anticipating the claimed method. Instead, another reference, Ballerstadt, is relied upon for rendering the format obvious for the interaction between a luminescent group and a quencher label leading to the proportional signal in the presence of analyte, as claimed. Therefore, the rejection is maintained.

Applicant's arguments regarding Ballerstadt are noted. However, while Applicant's arguments regarding the complex interactions of the elements in the method are noted, Applicant also noted that "only the P<sub>F</sub>R<sub>P</sub><sub>R</sub> complex... is a quenching effective complex" (p. 20 of remarks). Therefore, there are embodiments taught by Ballerstadt that render obvious the elements of the claim as currently recited. Furthermore, Therefore, in light of the arguments above regarding the

scope of the invention, Applicant's arguments are not persuasive over either Oh, Ballerstadt or Groopman.

Applicant traverses the rejection of claim 29 as being obvious over Oh, Ballerstadt, Groopman and Plowman. Applicant argues "Plowman does not cure the deficiency" and "Plowman et al. Do not describe tripods as claimed and a regeneration of a solid support" and "does not produce the claimed method" (p. 27 of remarks).

These arguments have been considered, but are not persuasive for the reasons stated above over the rejection of Oh, Ballerstadt and Groopman.

#### ***Pertinent Prior Art***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Miyazaki et al. (US Patent 5,229,302; July 1993) teaches a fluorescence immunoassay wherein the presence of analyte increases fluorescence that was previously quenched (Abstract).

#### ***Conclusion***

Claims 43 and 44 are free of the prior art. A thorough search of the prior art of the specific elected structure, Y2 and Y'2 was conducted and there was no disclosure in the prior art of the specifically elected structure. While the prior art teaches multifunctional reagents, the specific structure is not disclosed and would not have been an obvious structure based on the more general teachings in the prior art.

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Claims 43 and 44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 2829, 31-42 and 46 stand rejected. No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Stephanie K. Mummert/  
Examiner, Art Unit 1637

SKM

/GARY BENZION/  
Supervisory Patent Examiner, Art Unit 1637